The Evidence Base for Women

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Combination prevention to break the cycle of HIV transmission

**Men 25-40 years**
- Condoms
- Testing→ART for +men
- Partner testing
- VMMC for higher risk men

**Men<25ys**
- VMMC "plus" package
- Condoms
- Testing→ART for +

**Young women <25 years**
- PrEP
- Test & ART

**Women 25-40 years**
- PrEP for higher risk women
- Test & ART
- Partner testing

Changing community norms on age-disparate sex & patriarchy
WHO recommendation for PrEP

Oral PrEP (containing TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches:

- **Enabling recommendation**
- **Not population specific**
  - For people at substantial HIV risk (provisionally defined as HIV incidence > 3 per 100 person–years in the absence of PrEP)
- **Offer as an additional prevention choice**
- **Provide PrEP within combination prevention**
  - Condoms and lube
  - Harm reduction
  - HIV testing and links to ART
- **Provide PrEP with comprehensive support**
  - Adherence counselling
  - Legal and social support
  - Mental health and emotional support
  - Contraception and reproductive health services

- Modular
- Different audiences
- Different setting
- Different populations
- Suggestions not recommendations
- Much uncertainty
- Learn as implement
- Frequent updating anticipated

http://who.int/hiv/pub/prep/prep-implementation-tool
Recurrent concerns expressed by MoH

- **Cost**
  - Why should we prioritize PrEP when treatment is our immediate priority?

- **Where, Who**
  - Where do we start? Which populations? Where to offer services?

- **Safety**
  - 'Toxic drugs' for people without HIV
  - People taking PrEP, esp. with poor adherence: Will this result in lots of drug resistance?
  - Offering PrEP will mean people stop using condoms, have more sexual partners, more STIs
  - PrEP isn't safe during pregnancy and should be stopped when women become pregnant
  - What about drug interactions?

- **Drug resistance**
  - Lots of the trials had poor results with poor adherence

- **Behavioral disinhibition**
  - Many concerns esp. for adolescent girls e.g. safety, feasibility, adherence, perception of risk, parental consent

- **Pregnancy and hormonal contraception**
  - Many concerns esp. for adolescent girls e.g. safety, feasibility, adherence, perception of risk, parental consent

- **Adherence**
  - Many concerns esp. for adolescent girls e.g. safety, feasibility, adherence, perception of risk, parental consent

- **< 18 years**
  - Many concerns esp. for adolescent girls e.g. safety, feasibility, adherence, perception of risk, parental consent
PrEP and women – key issues

• Mixed "results" from trials

• Very little real world experience for women
  - Even less for adolescent girls
  - More (and increasing experience from sex worker projects)

• How to prioritize implementation
  - All women – overwhelming and unfeasible
  - Women at highest risk – often have multiple vulnerabilities
  - Women who want PrEP – may have self-identified high risk and more motivated to adhere
  - Balance between offering PrEP to women at substantial risk vs stigmatizing PrEP as something for 'risky women'

• Adherence is key
  - Good adherence in SDC trials and OLE
  - Poor adherence – commonly observed in other trials, esp younger women
  - Understanding poor adherence
  - Supporting better adherence

• Where to offer PrEP for women
  - ANC clinics, Family planning, STI services, Primary health care, ART clinics
Effectiveness of TDF and TDF/FTC antiretroviral pills & gels in women

Study

- **TDF2 – daily Tenovofir-Emtricitabine** (Women & Men - Botswana)\#
  - **Effect size (CI)**: 75%* (24; 94)

- **Partners PrEP – daily oral Tenofovir** (Discordant couples – Kenya, Uganda)
  - **Effect size (CI)**: 71%* (37; 87)

- **Partners PrEP – daily Tenovofir-Emtricitabine** (Discordant couples – Kenya, Uganda)
  - **Effect size (CI)**: 66%* (28; 84)

- **FEMPrEP – daily Tenovofir-Emtricitabine** (Women – Kenya, South Africa, Tanzania)
  - **Effect size (CI)**: 6% (-52; 41)

- **MTN003/VOICE – daily Tenovofir-Emtricitabine** (Women – South Africa, Uganda, Zimbabwe)
  - **Effect size (CI)**: -4% (-49; 27)

- **MTN003/VOICE – daily Tenofovir** (Women – South Africa, Uganda, Zimbabwe)
  - **Effect size (CI)**: -49% (-129; 3)

- **CAPRISA 004 – coital Tenofovir gel** (Women – South Africa)
  - **Effect size (CI)**: 39% (6; 60)

- **MTN003/VOICE – daily Tenofovir gel** (Women – South Africa, Uganda, Zimbabwe)
  - **Effect size (CI)**: 15% (-21; 40)

- **FACTS 001 – coital Tenofovir gel** (Women – South Africa)
  - **Effect size (CI)**: 0% (-40; 30)

\#(Study population and countries where the study was conducted)

*Effect size calculated from the incidence rate ratio for women only

Varying outcomes from PrEP trials - attributed to adherence
**PrEP ‘less forgiving’ for women compare to MSM**

Message: PrEP reaches effective steady state levels effectiveness after approximately 7 doses.

- **Protection likely to be adequate after 7 daily doses for women having vaginal sex** (PK studies from vaginal tissue)
- **Protected likely to be adequate after 7 daily doses for men having penile-vaginal sex** (very limited PK data from penile tissue) men
- **Protected likely to be adequate after <daily doses for anal sex** (PK studies from rectal tissue)

Event driven PrEP (eg Ipergay regime) shown from RCT to be effective for MSM – no studies for women – but unlikely to give adequate protection

“Time to effectiveness” in lower female genital tract (FGT) vs rectal tissue

## Multiple ongoing PrEP studies in young African women, including

<table>
<thead>
<tr>
<th>Study, funder, PIs</th>
<th>N &amp; locations</th>
<th>What it will teach us</th>
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| **HPTN 082/HERS** (NIH) Pis: Celum, Delaney-Moretlwe | 400 women ages 16-25 *(Harare, Joburg, & Cape Town)* | • Uptake;  
• Adherence with CBT counseling & 2 way SMS;  
• Effect of drug level feedback on adherence |
| **3Ps** (NIH & BMGF) Pis: Bekker, Celum | 200 women ages 16-25 *(Cape Town)* | • Uptake with creative marketing campaign;  
• Effect of incentives conditioned on drug levels on adherence |
| **POWER** (USAID) Pis: Baeten, Celum | 3000 women ages 16-25 *(Cape Town, Joburg, Kisumu)* | • Emphasis on scalable delivery models  
• Use of a decision support tool |
| **MTN 034 /REACH** Pis: Nair, Ngure, Celum | 300 women ages 16-21 *(Cape Town, Durban, Joburg, Harare, Kisumu)* | • Cross-over study to evaluate safety of oral TDF/FTC PrEP & dapivirine ring  
• Adherence  
• Preference of oral PrEP vs dapivirine ring |
PrEP in Pregnancy and BF: The rationale

- In some countries, PrEP discontinued when women at substantial HIV risk become pregnant
- HIV acquired during pregnancy/BF can be transmitted to infant
- In high prevalence settings, women at substantial HIV risk wishing to conceive may include those whose partners have HIV but are not virally suppressed, or whose status is unknown
Given the available safety data, there does not appear to be a safety-related rationale for discontinuing PrEP during pregnancy and breastfeeding for HIV-uninfected women receiving PrEP who become pregnant and remain at continuing risk of HIV acquisition.

In such situations, the risk of HIV acquisition and accompanying increased risk of mother-to-child HIV transmission appears to far outweigh the potential risk of fetal and infant exposure to TDF used for PrEP.

The final decision on whether to continue PrEP during pregnancy and breastfeeding should be made by the pregnant woman in consultation with her health care worker, balancing risks on HIV acquisition against potential harms.

Additional surveillance is important.
Feasibility, acceptability and safety of oral PrEP during pregnancy and breastfeeding in AGYW (16-24 years)

International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network

Observational cohort study of HIV-uninfected pregnant AGYW designed to

• characterize adherence over time among AGYW who initiate once daily PrEP during pregnancy & continue for 6 months following delivery
• compare pregnancy outcomes among women who take PrEP and women who decline PrEP during the AN period.
• Study sites in Zimbabwe, South Africa, Malawi, Uganda
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